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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/325,603 06/03/99 SVENDSEN

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EXAMINER

SLOBODYANSKY, E

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

10/14/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.  
**09/325,603**

Applicant(s)  
**Svendsen et al.**

Examiner  
**Elizabeth Slobodyansky**

Group Art Unit  
**1652**



☒ Responsive to communication(s) filed on Jun 18, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 71 and 72 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 71 and 72 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☒ received in Application No. (Series Code/Serial Number) 08/600,908

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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### **DETAILED ACTION**

The preliminary amendment filed concurrently with the specification inserting cross-reference to the related applications and SEQ ID NOs, replacing the Sequence Listing, canceling claims 1-70 and adding claims 71 and 72 has been entered with the following exception. The requested amendment on page 43, lines 2 and 9, has not been entered because it did not match the specification.

The supplemental preliminary amendment filed June 18, 1999 inserting "Brief Description of the Drawings" at page 4 has been entered.

Claims 71 and 72 are pending.

### ***Specification***

The disclosure is objected to because of the following. On page 4, "Figure 8" is recited instead of Figures 8A-8D; description of Figure 10 recites pJEN1 instead of pJeEN1. Correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 71 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a variant of a parent  $\alpha$ -amylase by modelling the parent  $\alpha$ -amylase on an X-ray crystallographic three-dimensional structure of  $\alpha$ -amylase having amino acid sequence of SEQ ID NO:13, does not reasonably provide enablement for a method of producing a variant of a parent  $\alpha$ -amylase by modelling the parent  $\alpha$ -amylase on an X-ray crystallographic three-dimensional structure of  $\alpha$ -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, or having a sequence at least 70% homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

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Factors pertinent to this discussion include predictability of the art, guidance in the specification, breadth of claims, and the amount of experimentation that would be necessary to use the invention.

In order to practice methods of claims 71 and 72 one skilled in the art would need an X-ray crystallographic three-dimensional structure of an  $\alpha$ -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, and 13 or having a sequence at least 70% homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13. Although the specification teaches the X-ray crystallographic three-dimensional structure of  $\alpha$ -amylase having amino acid sequence of SEQ ID NO: 13, it does not teach an X-ray crystallographic three-dimensional structure of an  $\alpha$ -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, or having a sequence at least 70% homologous to the sequences of SEQ ID NOs: 2, 4, 6, or 13. The field of the enzyme X-ray crystallography requires highly specialized skills, and is highly unpredictable. The state of the art disclose an X-ray crystallographic three-dimensional structure of no bacterial  $\alpha$ -amylase prior to the instant invention. In the prior art only the tree-dimensional structures of  $\alpha$ -amylases from *Aspergillus oryzae*(SEQ ID NO:10 in the instant specification), barley and pig pancreas are known.

Therefore, one of ordinary skill would require the information regarding an X-ray crystallographic three-dimensional structure of an  $\alpha$ -amylase having amino acid sequence of SEQ ID NOs: 2, 4, 6, or having a sequence at least 70% homologous to

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the sequences of SEQ ID NOs: 2, 4, 6, or 13, in order to make steps required by methods of claims 71 and 72 and use methods of claims 71 and 72 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 71 and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 71 and 72 recite "expressing the modified nucleic acid". It is unclear where said nucleic acid is expressed.

Claim 72 recites "an unrelated  $\alpha$ -amylase". It is unclear which  $\alpha$ -amylase can be considered unrelated.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claim 72 is rejected under 35 U.S.C. 103(a) as being unpatentable over MacGregor.

MacGregor (form PTO-1449) teaches a method of predicting an  $\alpha$ -amylase structure and properties using modelling a *Bacillus*  $\alpha$ -amylase on the known three-dimensional structure of  $\alpha$ -amylase from *Aspergillus oryzae*.

MacGregor teaches the method of analyzing an  $\alpha$ -amylase structure resulting in predictability residues important in various functions. MacGregor teaches the use of comparison of the amino acid sequences of any  $\alpha$ -amylase with the structure of an  $\alpha$ -amylase for which the tree dimensional structure is known in order to select positions for mutations. MacGregor teaches that position 44 in *B. amyloliquefaciens* (Termamyl-like  $\alpha$ -amylase, Seq ID NO 4 of the instant application) corresponds to position 66 in *Aspergillus oryzae* (non-Termamyl-like a-amylase, Seq ID NO 10 of the instant application) (page 404, figure 1) and that the length of the loop preceding tyrosine 82 of *A. oryzae* is shorter in *B. amyloliquefaciens* (page 412, 5th paragraph) and that this loop is positioned between residues 65 and 98 of *A. oryzae* (page 401, table I). Furthermore, MacGregor teaches that the length of loops (page 412, last paragraph through page 413) is responsible for an enzyme action pattern on amylose and binding the reducing end of the substrate.

With regard to calcium binding site MacGregor teaches residues participating in  $\text{Ca}^+$  binding (page 407, 4th paragraph through page 408, 2nd paragraph).

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MacGregor teaches that substitution of charged amino acids in the active site could lead to an altered pH dependency of an  $\alpha$ -amylase (page 410, Table III).

Therefore, MacGregor teaches a method corresponding to steps (a)-(c) in claim 72.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recombinantly produce a variant  $\alpha$ -amylase obtained using the detailed teachings of MacGregor discussed above. One skilled in the art would have been motivated to modify a nucleic acid encoding a known  $\alpha$ -amylase as required by claim 72 in step (d) in order to be able to recombinantly produce a variant  $\alpha$ -amylase as required by claim 72 in step (e). At the time the invention was made the production of an enzyme variant by expression of a nucleic acid in a host cell was by far the most common if not the only way of a variant production.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

  
Elizabeth Slobodyansky, PhD